
Single-cell RNA sequencing identifies diverse roles of epithelial cells in idiopathic pulmonary fibrosis.

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Authors: Yan Xu, Takako Mizuno, Anusha Sridharan, Yina Du, Minzhe Guo, Jie Tang, Kathryn A Wikenheiser-Brokamp, Anne-Karina T Perl, Vincent A Funari, Jason J Gokey, Barry R Stripp, Jeffrey A Whitsett

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Public Summary:

Idiopathic pulmonary fibrosis (IPF) is a lethal interstitial lung disease characterized by airway remodeling, inflammation, alveolar destruction, and fibrosis. We utilized single-cell RNA sequencing (scRNA-seq) to identify epithelial cell types and associated biological processes involved in the pathogenesis of IPF. scRNA-seq analyses identified loss of normal epithelial cell identities and unique contributions of epithelial cells to the pathogenesis of IPF. The present study provides a rich data source to further explore lung health and disease.

Scientific Abstract:

Idiopathic pulmonary fibrosis (IPF) is a lethal interstitial lung disease characterized by airway remodeling, inflammation, alveolar destruction, and fibrosis. We utilized single-cell RNA sequencing (scRNA-seq) to identify epithelial cell types and associated biological processes involved in the pathogenesis of IPF. Transcriptomic analysis of normal human lung epithelial cells defined gene expression patterns associated with highly differentiated alveolar type 2 (AT2) cells, indicated by enrichment of RNAs critical for surfactant homeostasis. In contrast, scRNA-seq of IPF cells identified 3 distinct subsets of epithelial cell types with characteristics of conducting airway basal and goblet cells and an additional atypical transitional cell that contributes to pathological processes in IPF. Individual IPF cells frequently coexpressed alveolar type 1 (AT1), AT2, and conducting airway selective markers, demonstrating "indeterminate" states of differentiation not seen in normal lung development. Pathway analysis predicted aberrant activation of canonical signaling via TGF-beta, HIPPO/YAP, P53, WNT, and AKT/PI3K. Immunofluorescence confocal microscopy identified the disruption of alveolar structure and loss of the normal proximal-peripheral differentiation of pulmonary epithelial cells. scRNA-seq analyses identified loss of normal epithelial cell identities and unique contributions of epithelial cells to the pathogenesis of IPF. The present study provides a rich data source to further explore lung health and disease.

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